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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/046,727	01/17/2002	Graham D. Cook	1142.0125-00	2584

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EXAMINER	
KIM, JENNIFER M	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/046,727	COOK ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-13 and 26-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-13,26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 9, 2007 has been entered.

Action Summary

The rejection of claims 6-13 and 26 under 35 U.S.C. 103(a) as being unpatentable over Sunshine et al. (U.S.Patent No. 4,522,826) of record in view of White (U.S.Patent No. 5,431,916) are hereby expressly withdrawn in view Applicants' persuasive argument. However, upon further consideration, a new ground(s) of rejection is made in view of Gullapalli (U.S.Patent No. 6,251,426 B1).

The rejection of claims 1 and 7-13 under 35 U.S.C. 103(a) as being unpatentable over Sunshine et al. (U.S.Patent No. 4,522,826) of record in view of Weng et al. (U.S.Patent No. 5,512,300) and further in view of Ouali et al. (U.S.Patent No. 6287600) is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claims 27-30 under 35 U.S.C. 103(a) as being unpatentable over Sunshine et al. (U.S.Patent No. 4,522,826) of record in view of Weng et al. (U.S.Patent No. 5,512,300) and further in view of Ouali et al. (U.S.Patent No. 6287600) and Drug Facts and Comparisons, 1997 Edition is hereby expressly withdrawn in view of Applicant's amendment.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6-13 and 26-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The newly add limitation "wherein

the ibuprofen is not enterically coated" was not literally or implicitly described with reasonable clarity in the claims or any other portion of the originally filed specification. The description does not convey with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention. This is a New Matter rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 6-9 and 26 are rejected under 35 U.S.C. 102(e) as being anticipated by Gullapalli (U.S.Patent No. 6,251,426 B1).

Gullapalli teaches liquid softgel filled formulations containing ibuprofen in free acid form and softgel capsules comprised of a gelatin sheath comprising ibuprofen and

polyethylene glycol. (abstract). Gullapalli teaches the formulation can have other ingredients such as diphenhydramine hydrochloride (an antihistamine). (column 2, lines 43-48, claims 5 and 17). Gullapalli teaches the effective dosage of ibuprofen be at least 175mg, and preferably about 200mg. (column 4, lines 28-30). These dosages are within Applicant's dosage set forth in claim 7 and preferred dosage of 200mg is same as recited amount in instant claim 8. Applicants' recitation in claims 6 and 26 of intended use for the employment in the sleep disturbances and the recitation of claim 6 of polyethylene glycol to prevent negative interactions between the ibuprofen and the diphenhydramine do not represent a patentable limitation in a composition claims since it fails to impart any physical limitation to the composition.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gullapalli (U.S.Patent No. 6,251,426 B1).

Gullapalli teaches liquid softgel filled formulations containing ibuprofen in free acid form and softgel capsules comprised of a gelatin sheath comprising ibuprofen and polyethylene glycol. (abstract). Gullapalli teaches the formulation can have other ingredients such as diphenhydramine hydrochloride (an antihistamine). (column 2, lines 43-48, claims 5 and 17). Gullapalli teaches the effective dosage of ibuprofen be at least 175mg, and preferably about 200mg. (column 4, lines 28-30). These dosages are within Applicant's dosage set forth in claim 7 and preferred dosage of 200mg is same as recited amount in instant claim 8. Gullapalli teaches the softgel capsule should be of a size that is easily swallowed and generally, the fill size of the capsule will be less than 600mg, and preferably about 500mg, or less in order for the capsule to be an acceptably small dimension. (column 4, lines 23-29). Gullapalli teaches the percentages of the formulation may also have up to 10% of an antihistamine, such as diphenhydramine hydrochloride. (column 2, lines 42-48).

Gullapalli teaches the amount of diphenhydramine hydrochloride expressed in percentages but does not teach the specific amounts in mg set forth in claims 10-13 and the specified citrate salt set forth in claims 12 and 13.

It would have been obvious to one of ordinary skill in the art to employ an amount of diphenhydramine up to 10% of preferred 500mg soft gel capsules taught by Gullapalli as preferred amount of diphenhydramine content because Gullapalli teaches that up to 10% diphenhydramine up to 50mg (10% of 500mg softgel) is useful as suggested by Gullapalli as an additional ingredient. One of ordinary skill in the art would have been motivated to employ diphenhydramine in any workable range up to 50mg in Gullapalli's

softgel composition in order to provide antihistamine effect addition to non-steroidal anti-inflammatory effect of ibuprofen for convenient single formulation comprising dual therapeutic effect. There is a reasonable expectation of successfully formulating 500mg softgel capsules that are easily swallowed by employing **up to 10% (up to 50mg)** of diphenhydramine because all the ingredients including active agents, binders, formulations are all well taught and suggested by Gullapalli.

Claims 1 and 7-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sunshine et al. (U.S.Patent No. 4,522,826) in view of Weng et al. (U.S.Patent No. 5,512,300).

Sunshine et al. teach a pharmaceutical composition comprising 50-400mg ibuprofen and from about 12.5-50mg diphenhydramine elicits an enhanced analgesic and/or anti-inflammatory response. (abstract, column 6, lines 44-45, column 7, lines 1-4, column 14, claim 39). Sunshine et al. also teach that polyethylene glycol is an acceptable carrier to the above composition (column 7, lines 31-35). Sunshine et al. teach the above composition can be formulated in **tablet form or two (bilayer) or more layered tablets.** (column 8, lines 4-10). Sunshine et al. teach that diphenhydramine is commercially available as the hydrochloride salt. (column 1, lines 60-65).

Sunshine et al. do not teach the separation of ibuprofen and diphenhydramine in different layers.

Weng et al. report that it has been recognized that solid dosage forms such as tablets containing ibuprofen and other ingredients tend to exhibit stability problems,

including the formulation of low melting point eutectics. (column 1, lines 13-20). Weng et al. report ibuprofen forms low melting point eutectics with diphenhydramine hydrochloride. (column 1, lines 55-57).

It would have been obvious to one of ordinary skill in the art to separate diphenhydramine and ibuprofen in different layers of Sunshine's two layered tablet (bilayer) because diphenhydramine and ibuprofen in a solid dosage forms such as tablets tend to exhibit stability problems including the formation of eutectics as taught by Weng et al. and because Sunshine teaches that the composition can be formulated in two or more layered tablets. One would have been motivated to separate ibuprofen and diphenhydramine bilayer tablet taught by Sunshine so that they be placed into physically discrete region of two different layers of bilayer tablet in order to avoid the eutectic stability problems of solid dosage form comprising diphenhydramine and ibuprofen reported by Wang et al. There is a reasonable expectation of successfully formulating Sunshine's two layered (bilayer) tablet by separating ibuprofen and diphenhydramine in order to achieve more stable bilayer tablet without the problems of forming an eutectic mixture.

Claims 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sunshine et al. (U.S.Patent No. 4,522,826) in view of Weng et al. (U.S.Patent No. 5,512,300) as applied to claims 1 and 7-13 and further Drug Facts and Comparisons, 1997 Edition, all of record.

Sunshine et al's teaching as applied as before and additional teachings as follows:

Sunshine et al. teach a pharmaceutical composition comprising 50-400mg ibuprofen and from about 12.5-50mg diphenhydramine elicits an enhanced analgesic and/or anti-inflammatory response. (abstract, column 6, lines 44-45, column 7, lines 1-4, column 14, claim 39). **Sunshine et al. teach that "propionic acid derivatives" including ibuprofen is defined as non-narcotic analgesics/nonsteroidal anti-inflammatory drugs having free –CH(CH3)COOH. (column 5, lines 1-20, particularly, lines 12-15).** Sunshine et al. also teach that polyethylene glycol is an acceptable carrier to the above composition (column 7, lines 31-35). Sunshine et al. teach the above composition can be formulated in tablet form or two or more layered tablets. (column 8, lines 4-10). Sunshine et al. teach that diphenhydramine is commercially available as the hydrochloride salt. (column 1, lines 60-65). **Sunshine et al. teach that the composition can be formulated with for oral administration in the form of tablets or capsules with any oral non-toxic pharmaceutically acceptable inert carrier such as lactose, starch cellulose and carboxymethylcellulose. (column 7, lines 15-45).**

Weng et al's teachings as applied as before.

Sunshine et al. and Weng et al. do not teach the onset of action of the composition of within 60 minutes.

Drug Facts and Comparisons teach that onset of action of antihistamines including diphenhydramine is within 15 to 30 minutes (page 1135, under Antihistamines: Dosage and Effects; page 1136 under Pharmacokinetics). Drug

Facts and Comparisons teach that onset of action of ibuprofen is 0.5 hour (30 minutes). (Page 1387, under pharmacokinetic parameters).

It would have been obvious to one of ordinary skill in the art that the bilayer tablet comprising ibuprofen and diphenhydramine taught by Sunshine et al. as modified by Weng et al. would have an effect within 60 minutes as claimed by the Applicants because Drug Facts and Comparison teaches that each of the active agents have onset of action within 30 minutes. It is expected that the combination of two agents would possess same onset of action as well-known by the cited reference.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

Response to Arguments

Applicants' arguments filed March 9, 2007 have been fully considered but they are not persuasive. Applicants argue that amended claims 1 and 27-30 by inserting "wherein the ibuprofen is not enterically coated" do not add new matter because the support is found in Example 2, page 11, lines 14-15, specification page 16, line 20 to page 27, line 3. This is not persuasive because such support is not recited or found in the specification. The cited pages, examples, and lines pointed by the Applicants in

instant specification has been carefully considered but it is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, **has possession** of the claimed invention, wherein "the ibuprofen is not enterically coated". The limitation was not literally or implicitly described with reasonable clarity in the claims or any other portion of the originally filed specification.

Applicant's arguments with respect to rejected claims 6-13 and 26 under 35 U.S.C. 103(a) unpatentable over U.S.Patent No. 4,522,826 ("Sunshine") in view of U.S.Patent No. 5,431,916 ("White") have been considered but are moot in view of the new ground(s) of rejection.

With regard to arguments regarding Sunshine reference, Applicants argue there is no teaching or suggestion in any of the cited references to modify their teachings to arrive at the claimed invention because Sunshine fails to specifically disclose the claimed composition including polyethylene glycol in combination with ibuprofen and diphenhydramine and it is improper for the Office to pick and choose polyethylene glycol from the list of binders in hindsight, as a mere list of compounds in Sunshine does not direct one of ordinary skill in the art to use polyethylene glycol. This is not persuasive because it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the

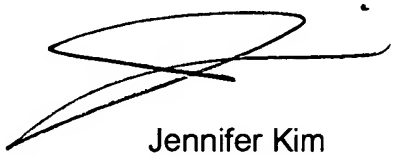
applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In this case, Sunshine teaches polyethylene glycol is a suitable binder to be employed in the composition comprising ibuprofen and diphenhydramine. Moreover, the employment of polyethylene glycol as a preferred agent to be combined with a formulation comprising ibuprofen and diphenhydramine is readily well-known by Gullapalli (U.S.Patent 6,251,426B1). Therefore one of ordinary skill in the art would have been motivated to employ well-known suitable binder, polyethylene glycol, well-known to be employed in the composition comprising ibuprofen and diphenhydramine by Sunshine and suitable for employing for the process of making such composition comprising the two actives. With regard to arguments regarding Quali reference have been considered but are moot in view of the new ground(s) of rejection. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Jennifer Kim
Patent Examiner
Art Unit 1617

Jmk
March 30, 2007